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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/045,116	10/23/2001	Henry Lamparski	348022000501	3354

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EXAMINER	
VOGEL, NANCY S	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 12/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/045,116	LAMPARSKI ET AL.	
	Examiner	Art Unit	
	Nancy T. Vogel	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36 and 43-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36 and 43-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/23/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 36 and 43-50 are pending in the case.

Continued Prosecution Application

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/23/04 has been entered.

The following is a new rejection:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 36, 43, 44, 46 and 47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a replication-competent adenovirus vector comprising a first and second adenovirus gene essential for replication wherein said first adenovirus gene is under transcriptional control of a carcinoembryonic antigen transcription regulatory element (CEA-TRE) wherein said CEA-TRE comprises a polynucleotide sequence within about –402 to about +69 nucleotides relative to the transcriptional start site of the CEA gene and a polynucleotide sequence including nucleotides from about –14.5 to about –3.8 kilobases or from about –6.1 to about –3.8 kilobases or from about –13.6 to about –10.6 kilobases relative to the transcriptional start site of the CEA gene. The claims are genus claims because they encompass polynucleotide sequences from any CEA transcription regulatory element, originating from any mammal. The specification has defined the term "CEA transcription regulatory element" as a polynucleotide sequence which comprises a CEA (carcinoembryonic antigen) gene promoter and enhancer. The specification discloses that the CEA-TRE may be isolated from any type of any mammal. There is no description of the specific structure that defines the genus as claimed, since as set forth above, the genus as claimed includes transcriptional regulatory elements, i.e. promoter and enhancer elements, from a large number of organisms, (i.e. any mammal), whose structures are not described. The disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one of skill in the art cannot envision all the adenovirus vectors comprising the recited carcinoembryonic antigen transcription regulatory elements. There is no structure-function analysis of the disclosed polynucleotide sequences which were isolated from human cells, whose sequence is

disclosed in the specification, to provide guidance on the essential regions of the promoter and enhancer regions isolated from other mammals, that would have the same function (i.e. transcriptional activity). Accordingly, in the absence of sufficient recitation of distinguishing characteristics, the specification does not provide adequate written description of the claimed genus which encompasses adenovirus vectors comprising CEA-TRE polynucleotides.

Vas-Cath V. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of CEA-TRE polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation or identification. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Col. Ltd.*, 18USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to

be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the disclosed adenovirus vectors comprising CEA-TRE polynucleotides isolated from human cells, whose sequence is set forth in SEQ ID NO:1 and Figure 2 (SEQ ID NO: 25), but not the full breadth of the claims, meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

The following is a new rejection:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 43-50 recites the limitation "said CEA enhancer" or "said CEA promoter" in the first lines of the claims. There is insufficient antecedent basis for this limitation in the claim on which they depend, i.e. claim 36. Claim 36 does not recite the terms "promoter" or "enhancer".

Claims 48-50 are vague and indefinite in the recitation of "nucleotides –402 to +69 as depicted in SEQ ID NO:1". The nucleotides in SEQ ID NO:1 range from [+] 1 to 471, and do not list any nucleotides using negative numbers. Therefore, it is unclear what nucleotides are intended in the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 36 and 43-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hallenbeck et al. (WO 96/17053) in view of Richards et al. (WO 95/14100).

This rejection is maintained essentially for the reasons made of record in the previous Office action, mailed 5/4/04.

In response, applicants have argued that Hallenbeck et al. disclose that "E1a or E1b gene may be operably linked to a tissue specific transcriptional regulatory and a vector which encodes a heterologous gene product that is toxic for the target tissue" and that "there is no teaching or suggestion that greater specificity or unexpected benefits could be obtained from the use of two different TREs to regulate a first and second adenovirus gene" (page 4 of the arguments). However, as has been previously argued, Hallenbeck et al. disclose that the disclosed preferred CEA regulatory sequence can be used to control more than one gene, and that E1A and E1B may be linked to separate tissue specific regulatory sequences (page 17, lines 5-6). Therefore, applicant's arguments regarding the Hallenbeck et al. teaching are not found convincing. Applicants further argue that the Hallenbeck et al. do not disclose the specific sequences disclosed in the instant application (page 5). However, it is maintained that Richards et al. disclose the human CEA enhancer sequences and their

use in regulating transcription in CEA producing cells. Applicants argue that Richards do not disclose the use of these sequences in adenovirus vectors for the cytolysis of target cells. (page 5). However, it is maintained that Richards et al. does suggest this use generally; at page 4, Richards states: "This [cell cytotoxicity] is achieved by the construction of a molecular chimaera comprising a "target tissue-specific" TRS that is selectively activated in target cells, such as cancerous cells, and that controls the expression of a heterologous enzyme. This molecular chimaera may be manipulated via suitable vectors and incorporated into an infective virion". Therefore, the general concept of selective expression of cytotoxic compounds in target cells using the disclosed enhancer and promoter sequences from the human CEA gene, are taught by Richards.

Applicant further bases arguments regarding unexpected advantages of the claimed invention on the Declaration of Dr. De-Chao Yu, submitted 8/4/04. These arguments are not found convincing for the following reasons.

The Declaration under 37 CFR 1.132 filed 8/4/04 is insufficient to overcome the rejection of claims 36 and 43-50 based upon Hallenbeck in view of Richards as set forth in the last Office action because:

The Declaration compares the effect of the presence of the human CEA enhancer on virus replication efficiency in adenovirus vectors comprising replication genes under the control of the CEA promoter. The results show increased selectivity of replication in CEA producing cells when the enhancer + promoter is present, vs. when only the promoter is present. However, it is maintained that Richards et al. disclose that

genes of interest will be specifically expressed in CEA producing cells when the CEA enhancer sequences, disclosed therein, are present (pages 3 (1/1)-4). Richards teaches the use of the disclosed CEA regulatory regions in virions, for the selective cytolysis of target cells (page 4). It is noted that applicant's representative has argued that the selective expression of genes under the control of the CEA enhancer + promoter, disclosed in Richards et al., is not as great as that shown in the Declaration of Dr. Yu. However, the experiments disclosed in Richards utilize different vectors, genes, cell types, experimental conditions, etc., than that utilized in the Declaration of Dr. Yu. Variations would have been expected, depending on such aspects as levels of cell specific factors, copy number, etc. Therefore, such a comparison is given little weight. The rejection is maintained.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy T. Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 6:30 - 3:00, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

TERRY MCKELVEY
PRIMARY EXAMINER